UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,271	03/08/2005	Alan Crossman	G & C 184.4-USWO	3503

22462 7590 03/04/2009

GATES & COOPER LLP
HOWARD HUGHES CENTER
6701 CENTER DRIVE WEST, SUITE 1050
LOS ANGELES, CA 90045

EXAMINER	
JAVANMARD, SAHAR	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
03/04/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,271	CROSSMAN ET AL.	
	Examiner	Art Unit	
	SAHAR JAVANMARD	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-37 and 39-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-37, 39-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

This Office Action is in response to applicant's arguments filed on 11/24/2008. Claim(s) 26-37, 39-45 and are examined herein.

Response to Arguments

In view of Applicant's amendments, the objection to claim 36 is hereby withdrawn.

Applicant's arguments with respect to the 112, first paragraph rejection of claim 50 has been fully considered but are not persuasive. The rejection is hereby maintained.

Applicant's arguments with respect to the 103(a) rejection of claims 26, 27, 30, 33-34, 36-37, 39 and 41-45 as being unpatentable over Chenard et al. (EP 0900568 A2) in view of Ling et al. (US Patent 6,200,970) have been fully considered but are not persuasive. The fact that both Chenard and Ling teach the administration of AMPA receptor antagonists for the treatment of Parkinson's disease, albeit different compounds, one of ordinary skill in the art would be motivated to at least try to employ the concept of treating dyskinesia with AMPA receptor antagonists as taught by Chenard and employed the AMPA receptor antagonists as taught by Ling.

Applicant contends that the compounds of formula I as defined in claim 26 are a different subset of 2,3-benzodiazepines from the AMPA receptor antagonists disclosed

in Ling which are not AMPA receptor antagonists. This argument is not persuasive because in fact the compounds encompassed by the instant claims are all within the scope of the compounds of formula I as taught by Ling. Additionally, Ling teaches said compounds as non-competitive inhibitors of AMPA receptors, which, as is well known in the art, are considered to fall under the definition of an antagonist.

Applicant's arguments with respect to the 103(a) rejection of claims 28, 29, 31, and 32 as being unpatentable over Chenard et al. (EP 0900568 A2) in view of Ling et al. (US Patent 6,200,970) as applied to claims 26, 27, 30, 33-34, 36-37, 39 and 41-45 above in further view of Solyom et al. (Current Pharmaceutical Design, May 2002) has been fully considered and are persuasive. The rejection is hereby withdrawn.

Applicant's arguments with respect to the 103(a) rejection of claim 35 as being unpatentable over Chenard et al. (EP 0900568 A2) in view of Ling et al. (US Patent 6,200,970) as applied to claims 26, 27, 30, 33-34, 36-37, 39 and 41-45 above in further view of http://web.archive.org/web/20000815082545/neurologychannel.com/parkinsonsdisease/index.shtml (referred to as "PD website" heretofore) has been fully considered but is not persuasive. Applicant argues that the "PD website" "provides no teaching of relevance to the presently claimed invention and certainly provides no teaching or suggestion to use a compound of the formula (I) to treat dyskinesias, let alone to specifically treat dyskinesias associated with idiopathic Parkinson's disease."

Examiner respectfully notes reference was not employed, nor ever suggested, to attempt to teach that compounds of formula I are used to treat dyskinesia. The website

reference was employed to address the limitation of claim 35 as to the specific type of Parkinson's disease, wherein the definition teaches that the most common type of Parkinson's disease is idiopathic Parkinson's disease.

Rejections that have been maintained have been restated for Applicant's convenience as well as new rejections are set forth in the following non-final office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 50 are rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling for the treatment of dyskinesia, does not reasonably provide enablement for the prevention/prophylactic treatment of dyskinesia as recited in these claims.

The instant claims are drawn to a method for the prevention/prophylactic treatment of dyskinesia. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention:

The instant invention pertains to a method for the prevention/prophylactic treatment of dyskinesia.

The state of the prior art:

The skilled artisan would view that the prevention/prophylactic treatment of one or more symptoms of dyskinesia totally, absolutely, or permanently, is highly unlikely, since one cannot guarantee that the dyskinesia will always be prevented.

The relative skill of those in the art:

The relative skill of those in the art is very high.

The predictability or lack thereof in the art:

The skilled artisan would view that preventing/prophylactically treating dyskinesia, absolutely or permanently, is highly unpredictable.

The amount of direction or guidance presented and the presence or absence of working examples:

In the instant case, no working examples are presented in the specification as filed showing how to prevent/prophylactic treat dyskinesia totally, absolutely, or permanently. Note that lack of a working example, is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.

Genentech, Inc. v. Novo Nordisk, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors, e.g., the amount of direction or guidance provided, absence of working examples, and the predictability of the art discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test the combination in the instant claims whether one can prevent/prophylactically treating dyskinesia totally, absolutely, or permanently.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 26, 27, 30, 33-34, 36-37, 39 and 41-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chenard et al. (EP 0900568 A2) in view of Ling et al. (US Patent 6,200,970).

Chenard teaches a method of treating dyskinesias associated with dopamine agonist therapy in the treatment of a CNS disorder, in particular Parkinson's disease through the administration of an AMPA receptor antagonist (page 2, lines 23-26).

Chenard teaches that dyskinesia means any abnormal or uncontrollable movement including chorea, tremor, dystonia, among others (page 10, lines 50-52).

Further, dopamine agonist therapy refers to therapy that increases dopamine receptor stimulation including bromocriptine and increasing levels of dopamine such as L-dopa among others (page 10, line 54-page 11, line 8).

Chenard does not teach the compounds of Applicant's formula I.

Ling teaches 2,3-benzodiazepines of formula I which are encompassed by Applicant's compounds of formula I (abstract; column 1, line 15- column 2, line 28). Ling teaches the compounds as being non-competitive inhibitors of the AMPA receptors (column 2, lines 30-32). Further, Ling teaches that the compounds can be used for treating neurological and psychiatric disorders that are triggered by overstimulation of the AMPA receptor. The neurological diseases, which can be treated functionally, include, for example, neurodegenerative disorders such as Parkinson's disease, Alzheimer's disease, and Huntington's chorea (column 3, lines 8-15).

It would have been obvious to one of ordinary skill in the art at the time of the invention to have treated dyskinesia with the administration of AMPA antagonists as taught by Chenard and employed the AMPA antagonists taught by Ling. One would be motivated to employ the compounds of formula I as taught by Ling because they are also taught to be useful in treating neurodegenerative disorders such as Parkinson's disease. Since both references teach the use of AMPA antagonists for treatment associated with Parkinson's disease, one would expect with a reasonable degree of success that the administration of one AMPA antagonist for another, namely the compounds employed by Ling, would be equally successful in treating dyskinesia, in the absence of unexpected results.

Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chenard et al. (EP 0900568 A2) in view of Ling et al. (US Patent 6,200,970) as applied to claims 26, 27, 30, 33-34, 36-37, 39 and 41-45 above in further view of

http://web.archive.org/web/20000815082545/neurologychannel.com/parkinsonsdisease/index.shtml (referred to as "PD website" heretofore).

Chenard and Ling are discussed above.

Neither Chenard nor Ling specifically teach the type of parkinsonism (i.e., idiopathic Parkinson's disease).

The "PD website" teaches that the most common type of Parkinson's disease is idiopathic Parkinson's disease because the cause is unknown.

It would have been obvious to one of ordinary skill in the art at the time of the invention that employing the treatment of dyskinesia associated with parkinsonism as discussed above, that one would have necessarily been treating idiopathic Parkinson's disease. The motivation, provided by the PD website, teaches that idiopathic Parkinson's disease is the most common type of the disease.

Claims 26-34, 36, 37, and 39-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leventer (US Patent No. 6,649,607 B2) in view of Chenard et al. (EP 0900568 A2).

Leventer teaches the administration of S-tofisopam for the treatment of convulsions or seizures selected from Parkinson's disease, other neurodegenerative diseases including Huntington's disease, schizophrenia, tics (e.g., Tourette's syndrome), head injury, among others (column 3, line 65-column 4, line 10).

Further, Leventer teaches that S-tofisopam can be administered alone or in combination with one or more other anti-convulsant agents to treat convulsions or seizures including myoclonic jerks (i.e., clonic activity) (column 9, lines 45-49).

Leventer does not specifically teach treating dyskinesia per se. Leventer also does not teach that the convulsions or seizures arising from Parkinson's or Tourette's syndrome, for example, are a result of dyskinesia associated with dopamine agonist therapy.

As taught by Chenard, dyskinesia is defined as any abnormal or uncontrollable movement including chorea, tremor, dystonia, athetosis, myoclonus and tic (page 10, lines 50-52).

Furthermore, as is well known in the art and also taught by Chenard, dyskinesia is a side effect that results from dopamine agonist therapy in an effort to treat Parkinson's disease (page 2, lines 21-23).

As taught by Chenard, dopamine agonist therapy refers to therapy that increases dopamine receptor stimulation including bromocriptine and increasing levels of dopamine such as L-dopa among others (page 10, line 54-page 11, line 8).

It would have been obvious to one of ordinary skill in the art at the time of the invention to have employed the administration S-tofisopam for the treatment of convulsions or seizures selected from Parkinson's disease, other neurodegenerative diseases including Huntington's disease, schizophrenia, tics (e.g., Tourette's syndrome) and head injury as taught by Leventer and also used it to treat dyskinesia. As taught by Chenard, dyskinesia is defined as any abnormal or uncontrollable movement including

chorea, tremor, dystonia, athetosis, myoclonus and tic. Thus by administering S-tofisopam, one in essence would have been treating the symptoms that arise from the ailments taught by Leventer of which are specific to dyskinesia, a few of which include tics and myoclonic jerks.

Additionally, it would have also been obvious to have administered S-tofisopam for the treatment of dyskinesia as discussed above and also employed the administration of S-tofisopam to treat dyskinesia that arises from an agent that is used to treat Parkinson's disease, namely dopamine agonists. One would be motivated to treat dyskinesia with the administration of S-tofisopam regardless of whether the dyskinesia results from the actual symptoms of a disease, specifically tics arising from Tourette's syndrome, or whether the dyskinesia is a side effect observed upon administration of an agent used to treat a particular disease, namely dopamine agonist therapy for Parkinson's disease.

Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Leventer (US Patent No. 6,649,607 B2) in view of Chenard et al. (EP 0900568 A2) as applied to claims 26-34, 36, 37, and 39-45 above in further view of http://web.archive.org/web/20000815082545/neurologychannel.com/parkinsonsdisease/index.shtml (referred to as "PD website" heretofore).

Leventer and Chenard are discussed above.

Neither Leventer nor Chenard specifically teach the type of parkinsonism (i.e., idiopathic Parkinson's disease).

The "PD website" teaches that the most common type of Parkinson's disease is idiopathic Parkinson's disease because the cause is unknown.

It would have been obvious to one of ordinary skill in the art at the time of the invention that employing the treatment of dyskinesia associated with parkinsonism as discussed above, that one would have necessarily been treating idiopathic Parkinson's disease. The motivation, provided by the PD website, teaches that idiopathic Parkinson's disease is the most common type of the disease.

Conclusion

Claims 26-37, 39-45 and 50 are not allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sahar Javanmard whose telephone number is (571) 270-3280. The examiner can normally be reached on 8 AM-5 PM MON-FRI (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/S. J./

Examiner, Art Unit 1617

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617